Post Synthetic Metal Extraction into Nanoparticles Reduces Preparation Time and Enhances Payload for Bimodal Imaging Probes

Edith Amason[1, 2], Durva Patel[1]; Emily Que Ph.D.[1] and Eszter Boros Ph.D.[2]

[1]Department of Chemistry, College of Natural Sciences, The University of Texas at Austin; [2]Department of Chemistry, College of Letters and Science, University of Wisconsin-Madison

The University of Texas at Austin
Department of Chemistry
College of Natural Sciences

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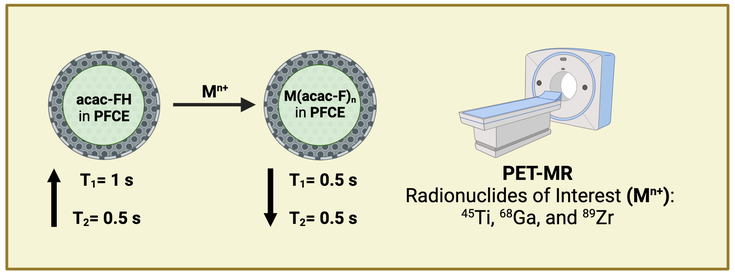
Demand for a PET-MR Probe

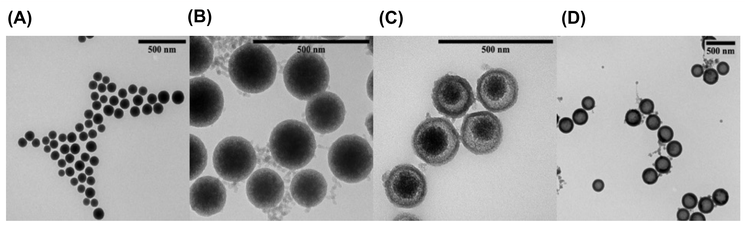


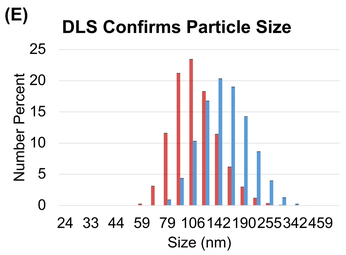
The implementation of hybrid imaging instruments, specifically the PET-MR, in clinical practice demands for the synthesis of a probe with optimized functionality for both imaging types. While there is significant literature precedent for small molecule and nanoprobes for the respective imaging modalities, little work has been conducted into the development of a dual imaging probe.[1,2] *I hypothesize that mesoporous silica nanoparticles **(MSNs),** containing a fluorous extractant, will enable rapid aqueous radiometal ion chelation inside of the MSNs addressing the challenges of PET-MR imaging.* This proof-of-concept study will include:

- Synthesis and full characterization of fluorous MSNs with the extractant (perfluoroheptanoyl)acetone **(acac-FH)** in perfluorocrown-5-ether **(PFCE)**[3,4]
- Experimental design and optimization the extraction of iron(III) citrate
- Radiolabeling with PET isotopes and phantom images for PET-MR

This work seeks to use the information gained from iron extraction to improve upon the lengthy synthesis times associated with nuclear medicine, and the direct competition with the desirable short half-lives of medically relevant isotopes. Although the current scope of future work is focused on the implementation of imaging isotopes like ^{45}Ti ($t_{1/2}$= 3 hr), ^{68}Ga ($t_{1/2}$= 68 min), and ^{89}Zr ($t_{1/2}$= 78 hr); there is great potential for the application of this system as a theranostic probe.[5]

Characterization of Fluorous MSNs



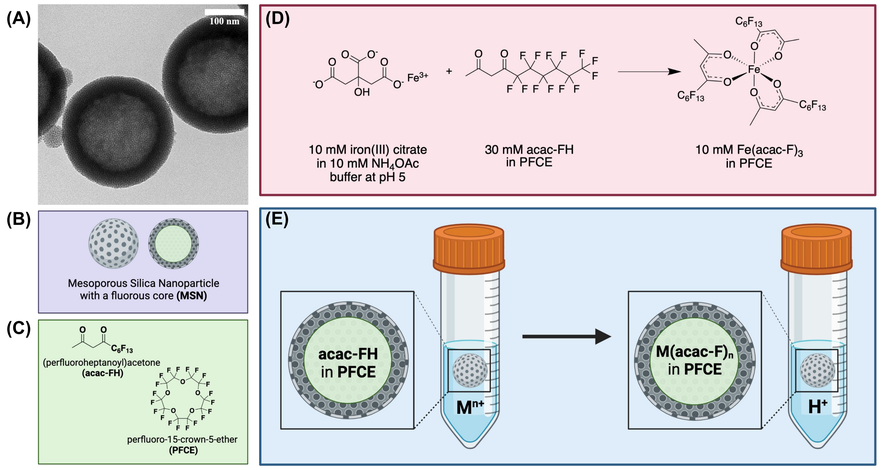


(F)

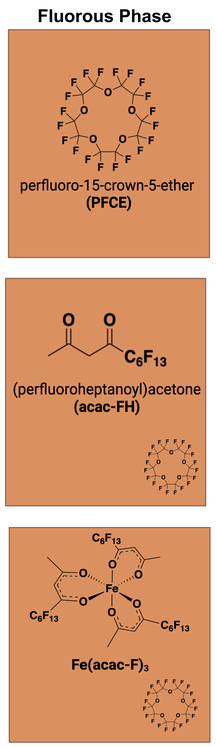
Sample	Z-Average (nm)	PDI
$dSiO_2$	136.96 +/- 9.30	0.052
MSN	178.10 +/- 11.29	0.051

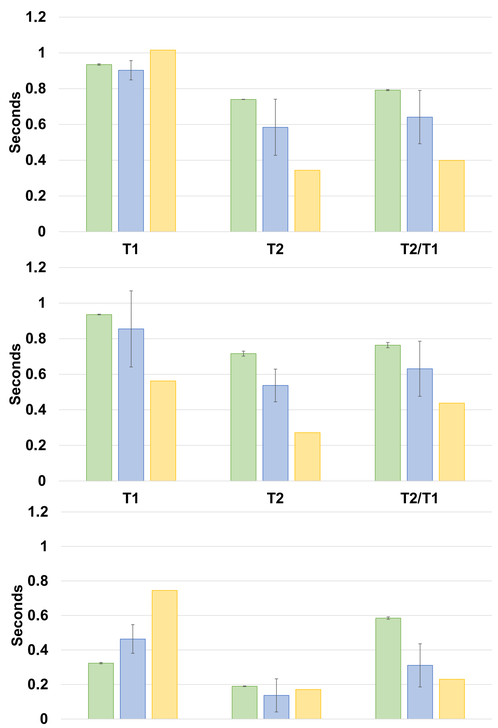
A full characterization of the MSNs is conducted prior to addition of fluorous phase. Transmission electron microscopy images depict the stages of MSN synthesis starting with the $dSiO_2$ (dense silica cores) **(A),** the addition of the mesoporous shell **(B),** partial etching of the dense silica cores **(C)** and completed synthesis of hollow MSNs **(D)**. Dynamic light scattering **(DLS)** is used after the synthesis of the silica cores and after the addition of the mesoporous shell, when overlain there is a clear shift of approximately 40 nm **(E),** from this data the Z-average and polydispersion index **(PDI)** are calculated **(F).**

Post Synthetic Extraction of Metal Ions into MSNs



MSNs extract iron into core post synthetically. MSNs of approximately 150 nm in size **(A)** are loaded with the fluorous phase by sonication **(B,C).** The nanoparticles are dispersed in buffer containing iron(III) citrate and are left under sonication to promote the extraction of the aqueous iron citrate into the fluorous phase, forming the $Fe(acac\text{-}F)_3$ complex **(D)** in the core of the MSN **(E)**. After a series of washes to remove excess iron, ^{19}F- NMR spectroscopy is utilized to determine if iron has successfully been extracted into the fluorous phase.





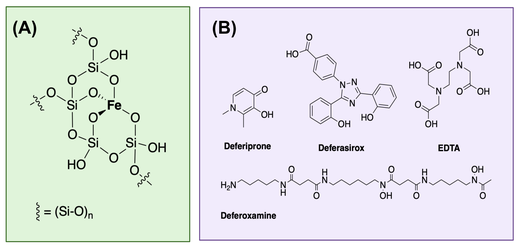
^{19}F- NMR confirms that adding the fluorous phase to MSNs does not alter the relaxation time.

MSNs with acac-FH have a noticeable decrease in T_1 and T_2 after the addition of iron(III) citrate to the solution.

Additional iron is not extracted into the fluorous phase after the initial extraction.

**Relaxation times are measured by ^{19}F-NMR with respect to PFCE by standard Inversion Recovery and CPMG experiments

Improving Selective Metal Ion Extraction

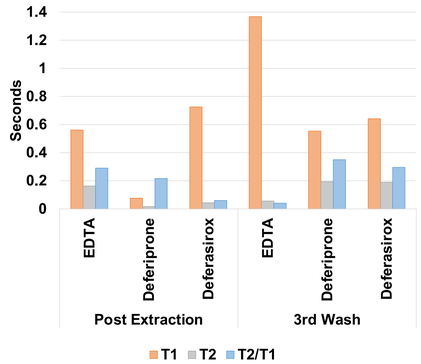


Iron is extracted into MSNs but remains on outer silica shell.

- Silica bound iron alters T_2 relaxation times **(A)**
- Potential iron chelators for exploration as washing agents **(B)**.

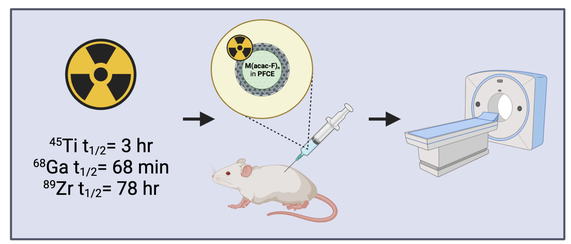
Known iron chelators have varying results eliminating MSN shell bound iron.

- EDTA shows the least promising results with iron removed from the fluorous phase and left on the particles
- Deferasirox shows the most promise removing shell bound iron without competing for fluorous iron



Future Work Incorporating Radiometals

After radiolabeling experiments have been optimized there is potential for in vivo work to be conducted and for dual ^{19}F MR-PET images to be acquired.



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Acknowledgements

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